HANDOUT 1

Arkansas PANS/PANDAS Advisory Council Meeting

Monday, March 9, 2020
3:30pm
Room B, MAC
Little Rock, Arkansas

Childhood Post-infectious Autoimmune Encephalopathy (CPAE) Clinic
March 9, 2020

Table of Contents:

- *page 1* — "Introduction to the CPAE Clinic" and "Diagnostic Criteria for PANS"
- *page 2* — "Differentials" – summarizes a list of possible explanations for the presenting symptoms.
- *page 3* (top section) — "Pre-appointment Lab Requirements" – results provide important information to aid with ruling out/in various differentials.
- *page 4* — "Clinic Process" – outlines the process of integrating family history, medical history, symptoms, physical exam, psychiatric assessment, mental status, neurological exam, and labs results in order to reach a diagnosis and plan of care.
  A "Diagnostic Category/Code" is decided upon after thorough assessment and discussion by the treatment team.
- *page 3* (bottom section) — Lists a brief description of "Diagnostic Categories/Codes" 1A, 1B, 2A, 2B, 2C, and 3.
- *page 5* — "Diagnostic Categories/Codes and Treatment Approach" – outlines CPAE Tiered Treatment according to the Diagnostic Category/Code
- *page 6* — "Treatment Process" – explains the follow up process
- *pages 7 and 8* — "Course of Illness at Clinic Entry" – outlines possible phases of illness

Childhood Post-Infection Autoimmune Encephalopathy (CPAE) Clinic

A multidisciplinary clinic formed by collaboration between University of Arkansas for Medical Sciences (UAMS) and Arkansas Children's Hospital (ACH)

A diagnosis of Childhood Post-Infectious Autoimmune Encephalopathy (CPAE) is made when a child's clinical history is consistent with consensus guidelines for Pediatric Acute-onset Neuropsychiatric Syndrome (PANS) (Chang et al. 2014).

Pediatric Acute-onset Neuropsychiatric Syndrome (PANS) Diagnostic Criteria:

I. Abrupt, dramatic onset of (1) obsessive-compulsive disorder or (2) severely restricted food intake (Neuropsychiatric symptoms flare to maximum intensity within 72 hours of symptom onset).

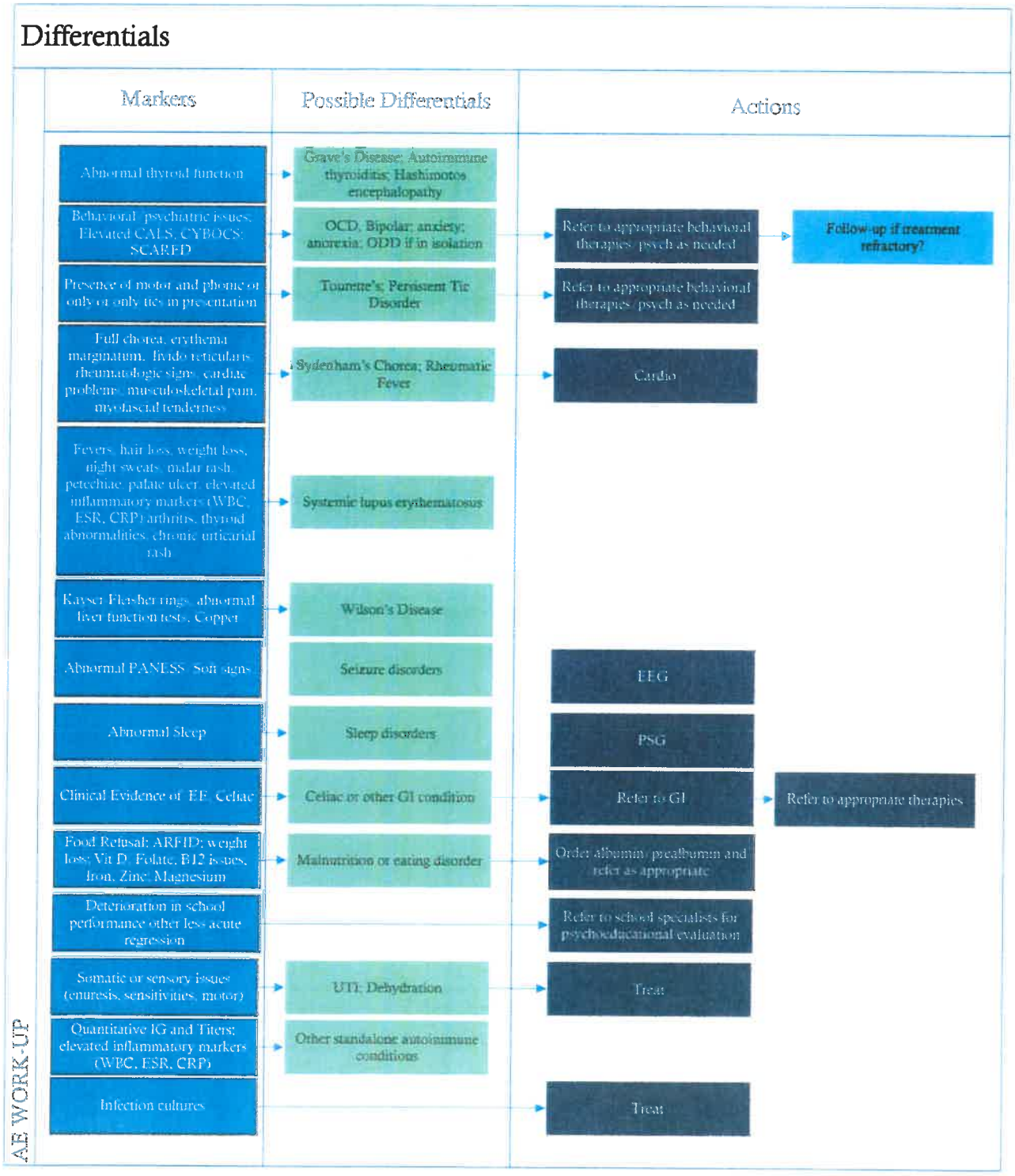
II. Concurrent presence of additional neuropsychiatric symptoms, (with similarly severe and acute onset), from at least two of the following seven categories:

1) Anxiety
2) Emotional lability and/or depression
3) Irritability, aggression, and/or severely oppositional behaviors
4) Behavioral (developmental) regression
5) Deterioration in school performance (related to attention deficit/hyperactivity disorder (ADHD-like symptoms, memory deficits, cognitive changes)
6) Sensory or motor abnormalities
7) Somatic signs and symptoms, including sleep disturbances, enuresis, or urinary frequency

III. Symptoms are not better explained by a known neurologic or medical disorder, such as Sydenham chorea, Tourette disorder, systemic autoimmune disease, or others.

The CPAE clinical evaluation of PANS closely follows the guidelines contained in the consensus statement on this topic published by Change et al. 2015.

"...It should be noted that PANS is a "diagnosis of exclusion" and that other known medical diseases must be ruled out before a diagnosis of PANS is assigned..."


Differentials
Markers
Possible Differentials
Actions
AE WORK-UP
Abnormal thyroid function
Grave's Disease; Autoimmune thyroiditis; Hashimotos encephalopathy
Behavioral/psychiatric issues. Elevated CALS, CYBOCS; SCARED
OCD, Bipolar; anxiety; anorexia; ODD if in isolation
Refer to appropriate behavioral therapies/psych as needed
Follow-up if treatment refractory?
Presence of motor and phonic or only or only tics in presentation
Tourette's; Persistent Tic Disorder
Refer to appropriate behavioral therapies/psych as needed
Full chorea, erythema marginatum, livido reticularis, rheumatologic signs, cardiac problems, musculoskeletal pain, myofascial tenderness
Sydenham's Chorea; Rheumatic Fever
Cardio
Fevers, hair loss, weight loss, night sweats, malar rash, petechiae, palate ulcer, elevated inflammatory markers (WBC, ESR, CRP) arthritis, thyroid abnormalities, chronic urticarial rash
Systemic lupus erythematosus
Kayser Fleisher rings, abnormal liver function tests, Copper
Wilson's Disease
Abnormal PANESS, Soft signs
Seizure disorders
EEG
Abnormal Sleep
Sleep disorders
PSG
Clinical Evidence of EF, Celiac
Celiac or other GI condition
Refer to GI
Refer to appropriate therapies
Food Refusal; ARFID; weight loss; Vit D, Folate, B12 issues, Iron, Zinc, Magnesium
Malnutrition or eating disorder
Order albumin/prealbumin and refer as appropriate
Deterioration in school performance other less acute regression
Refer to school specialists for psychoeducational evaluation
Somatic or sensory issues (enuresis, sensitivities, motor)
UTI; Dehydration
Treat
Quantitative IG and Titers; elevated inflammatory markers (WBC, ESR, CRP)
Other standalone autoimmune conditions
Infection cultures
Treat

Pre-Appointment Labs Requirements

Anti-Streptolysin O (ASO) and Anti-DNAse B
CBC with Manual Diff
Celiac Panel (tissue transglutaminase antibody tTG)
CMP including liver functions
Copper and Ceruloplasmin
C-Reactive Protein (CRP)
Erythrocyte Sedimentation Rate (ESR)
Iron Panel (ferritin, TIBC)
Quantitative IG Panel (IgG, IgM, IgA, IgE) and IgG subclasses
RBC magnesium and folate
Throat Culture (Strep and mycoplasma)
Thyroid Function Panel (TSH, T4, Anti Thyroperoxidase (TPO), Thyroglobulin Antibody)
Titers: ANA, streptococcus, pneumoniae, diptheria/tetanus
Urinalysis (Hydration and rule out UTI)
Vitamins B12, 2 25-OH

Pre-Appointment Intake Forms

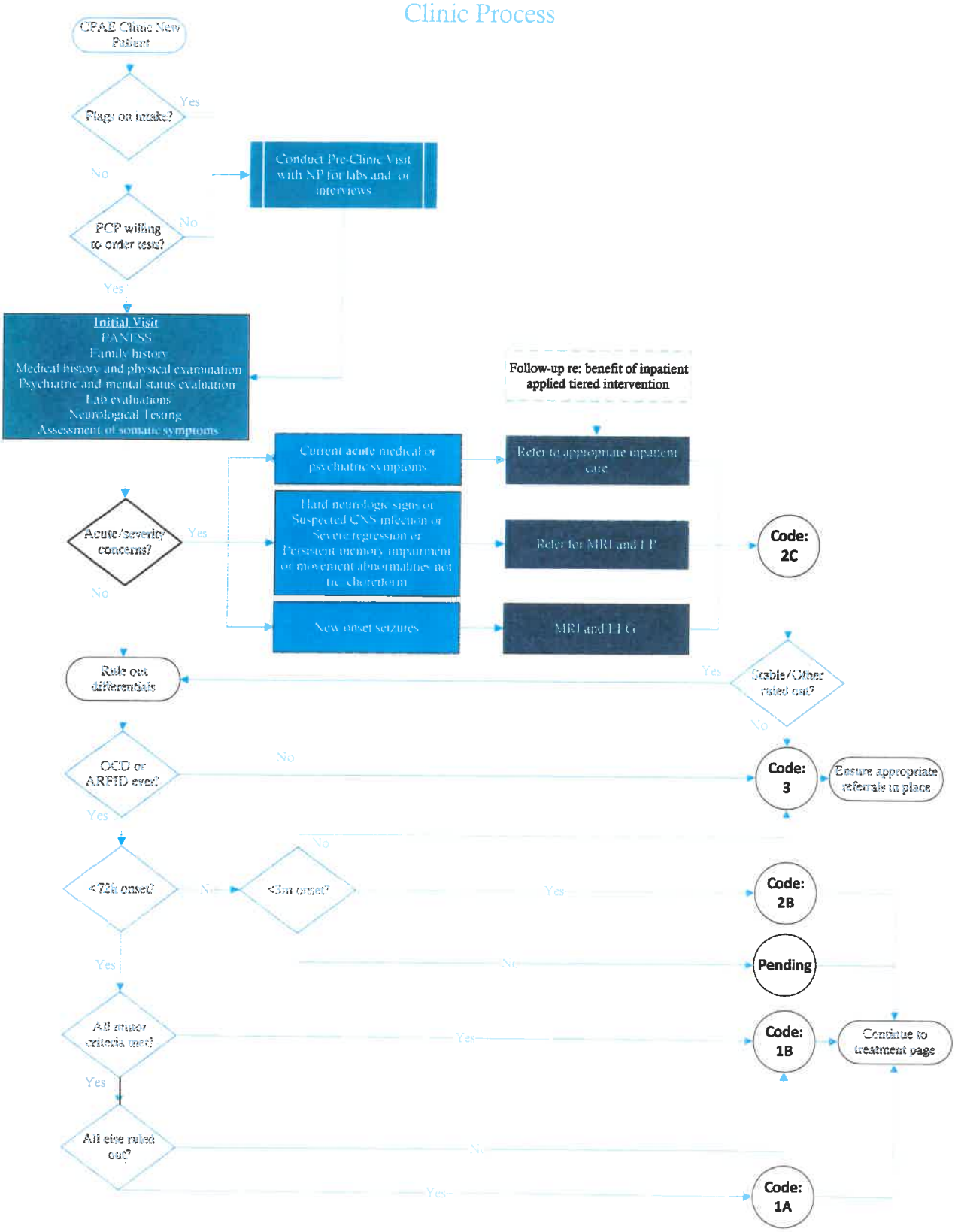
Intake Form
SCARED (parent and child)
OCI-CV (parent and child)
CALS (parent and child)
Vanderbilt
NIAS (parent and child)
ACES (parent and child)

Pre-Clinic Interviews

Positive SCARED → PARS
Positive CALS → CDRS-R
Positive OCI → CYBOCS
Positive NIAS → EAT

1A	DEFINITE PANS: All major and minor criteria met; all differentials ruled out
1B	PROBABLE PANS: All major criteria met
2A	POSSIBLE PANS: OCD or ARFID met without subacute onset or OCD/ARFID presenting with later flare
2B	OTHER SUBACUTE NEUROPSYCHIATRIC: Criteria not met but with acute or subacute (<3m)onset
2C	OTHER NEUROPSYCHIATRIC: Criteria not met but responsive to treatment
3	RULE OUT: Differential diagnosis or unknown diagnosis not appropriate for CPAE treatment

Clinic Process



Diagnostic Categories/Codes and Treatment Approach:

!! Category/Code 0 !!: The patient is in crisis and needs a higher level of care, either medical or psychiatric. It is important to review criteria for Autoimmune Encephalitis and refer to appropriate treatment. The patient may return to outpatient treatment after stabilization.

Special notes on neurologically concerning symptoms:

A) Atypical neurological findings are considered neurological symptoms other than tics, motoric hyperactivity, mild to moderate handwriting changes, or mild choreiform movements.

B) Attention to diagnostic criteria for possible autoimmune encephalitis (Graus and Mooneyham) is essential in the evaluation of all possible CPAE cases.

Diagnosis of possible autoimmune encephalitis can be made when all three of the following criteria have been met:

1. Subacute onset (rapid progression of less than 3 months) of working memory deficits (short-term memory loss), altered mental status (decreased or altered level of consciousness, lethargy, or personality change), or psychiatric symptoms

2. At least one of the following:

- *New focal CNS findings*
- *Seizures not explained by a previously known seizure disorder*
- *CSF pleocytosis (white blood cell count of more than five cells per mm3)*
- *MRI features suggestive of encephalitis*

3. Reasonable exclusion of alternative cause

Category/Code 1A, 1B, 2A, 2B or 2C: If criteria are met for definite, probably, or possible PANS, then CPAE Tiered Treatment interventions are begun, such as anti-inflammatory medications and/or antibiotics.

CPAE Tiered Treatment Protocol

To manage frequent flares associated with infections follow the tiered interventions. This plan may be changed for a child's individual needs. It is our general approach that we are less likely to move to higher risk interventions when a patient is further down on the Classification System.

1. PCP to check for strep or other infection and treat according to results.

2. Start an NSAID - Naproxen (Aleve) (10 mg/kg/dose - max dose 220mg) twice daily for 4 weeks. If taking Naproxen (Aleve) or another NSAID regularly it is important to protect and monitor the GI tract by:

- *Repeating labs every 3 months: CMP/CBC, Urinary Analysis and Stool hemoccult*
- *Adding a probiotic – Culturelle Kids Chewable (1 tablet daily)*
- *Adding a proton pump inhibitor*

3. Add or change to Azithromycin 250 mg every MWF for 4 weeks if there is no improvement with NSAID during a flare.

4. Consider adding or change to Prednisone (1-2 mg/kg/day – max dose 40mg/day) daily for 5 days if there is no improvement with above interventions during a flare.

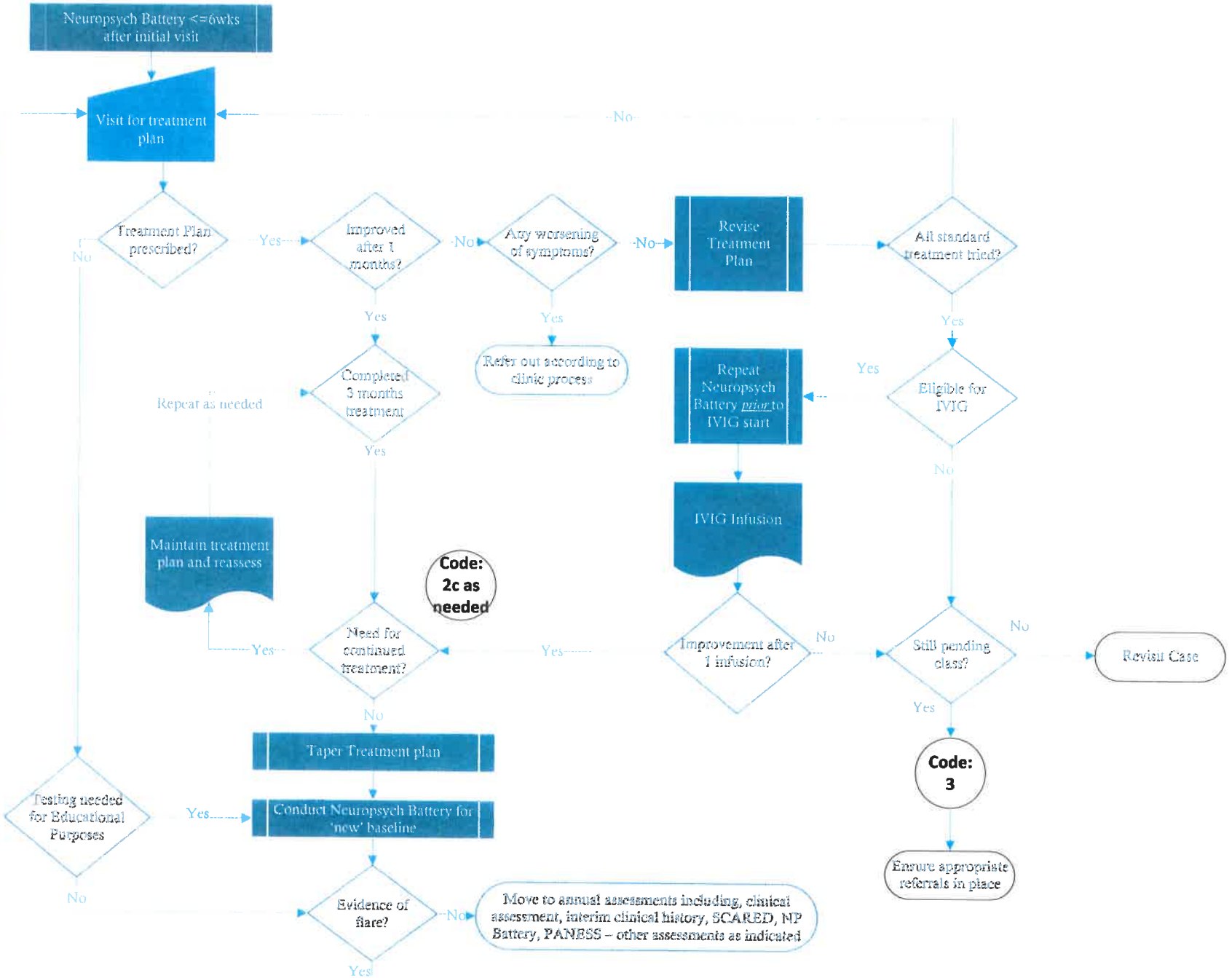
5. If child is doing well, start weaning medications as tolerated.

6. Patient to be actively engaged in psychological/behavioral therapy.

7. Parent to call every 4 weeks to update clinic when above interventions have been implemented.

Category/Code 3: PANS/PANDAS ruled out and no evidence of autoimmune, inflammatory, or metabolic disorder. Refer for appropriate treatment of psychiatric and/or medical disorders.

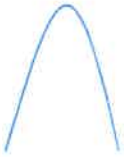
Treatment Process



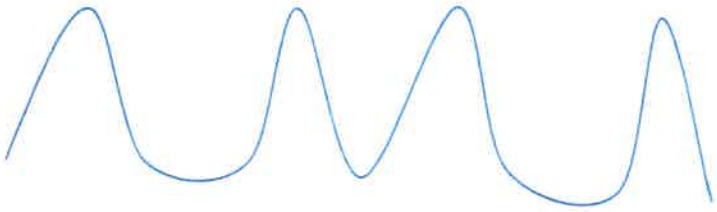
Updated on 4/8/3019

Course of illness at clinic entry

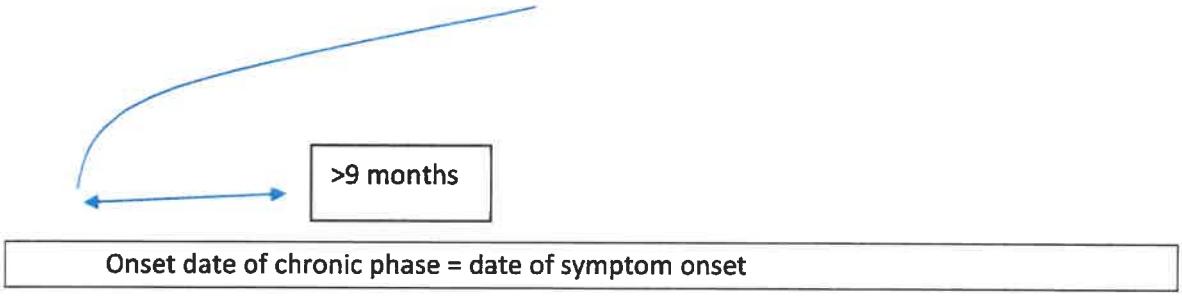
1. New single episode



2. Relapsing remitting (≥2 episodes meeting PANS criteria with each episode ≥6 weeks)



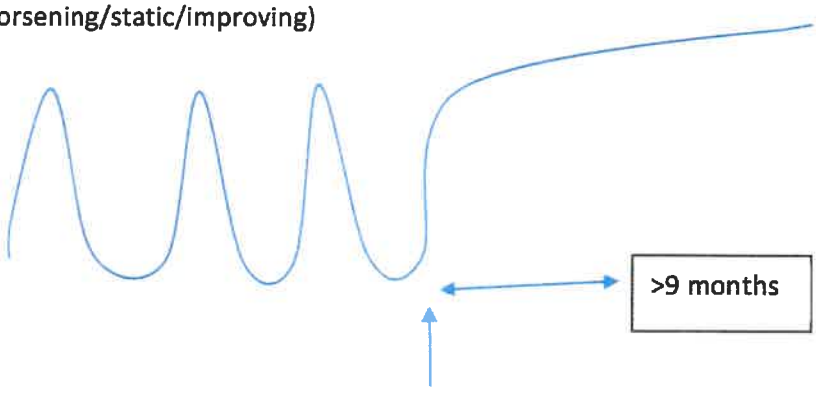
3. Primary chronic (symptoms never spontaneously improve (resolution phase) without aggressive treatment). At time of clinic entry and/or research draw, trajectory of chronic symptoms defined as worsening, static, or improving.



If aggressive medical treatment (IVIG, IV steroids, Ritux, etc) within 9 months of onset AND

- If patient improves significantly → Natural course unknown therefore the patient is not classifiable.
- If patient does not improve → Primary chronic

4. Secondary chronic (started with relapsing remitting, then chronic) → trajectory (worsening/static/improving)



Onset date of chronic phase

Chronic state = ongoing symptoms (?GI >40, moderate impairment) for a continuous 9 months.

Onset date of chronic state = start date of the chronic phase

Pre-PANS episodes (any PANS symptom lasting ≥1 week; problem – difficult to quantify)

Future study topics

Course of illness at 1 year, 2 years and 5 years

References

Ref. Lublin FD et al. Defining the clinical course of multiple sclerosis: the 2013 revisions. Neurology. 2014;83(3):278-86.

INTERIM PHONE NUMBER FOR

ACH/UAMS CPAE CLINIC

REFERRALS:

501-364-3416